

TOXIC NEPHRITIS DEPENDENT UPON SURGICAL CONDITIONS.*

BY NATHAN JACOBSON, M.D.,

OF SYRACUSE, N. Y.,

Professor of Surgery in Syracuse University; Surgeon to St. Joseph's Hospital.

It is not the purpose of this paper to discuss all of the toxic agencies capable of producing nephritis. This is the work of the physician rather than the surgeon.

As long ago as 1874, Vulpian¹ gave expression to the thought that the elimination of vicious products caused by the incomplete or abnormal function of our organs was frequently responsible for irritation of the kidneys and in turn could produce parenchymatous nephritis. To Bouchard, whose first work appeared in France in 1887 and which was subsequently translated and published in this country in 1894, we owe, however, much of our knowledge of the disturbances caused by autointoxication. French, German and Italian investigators and clinicians have given this subject extensive study.

In 1895, there appeared in the *Gazette des Hopitaux* a paper by Gouget,² in which he enumerated the various forms of nephritis dependent upon toxic conditions. Amongst the diseases and conditions thus held responsible he included gout, diabetes, chlorosis, the cachexias, arteriosclerosis, disturbances of the gastro-intestinal tract, pregnancy, hepatic diseases with and without jaundice, myxœdema, exophthalmic goitre and lesions producing suppression of the functions of the skin.

At the Göttingen clinic between 1897 and 1900, 142 cases of nephritis were observed. In 109 the etiology was apparently determined. Of the infectious diseases typhoid was the most common cause, being responsible for 24 of the cases. Scarlet fever, articular rheumatism, diphtheria, influenza, pneu-

* Read before the Medical Society of the State of New York, January, 1907.

monia and tuberculosis were amongst the other infections responsible for this condition.

It has long been known that in septicæmia nephritis is a frequent manifestation. However, the surgical conditions which are capable of producing pathologic changes in the kidneys have not been very carefully studied in the English speaking countries.

It is still an open question whether the presence of bacteria in the urine implies a diseased condition of these organs or whether bacteria can be eliminated by the kidneys without producing any pathologic change in them. The question has arisen whether in this form of nephritis the provoking cause is the bacteria, themselves, or the toxins produced by them.

The experimental work of Pernice and Scagliosi³ shed considerable light on this subject. They experimented with guinea pigs, rabbits and dogs. Bouillon cultures from several microorganisms were used. Histologic examination was made of the kidney tissue while it still possessed living body-warmth, as well as of sections subsequently hardened and again having been boiled for one minute. The animals experimented upon were killed at periods of two, four or six hours after infection and so on up to twenty-four hours. Others were allowed to live forty-eight or sixty hours and some as long as fifteen days after inoculation. The existing conditions at these specified times were carefully studied. The bacillus of anthrax, as well as the bacillus pyocyaneus and the staphylococcus pyogenes aureus were used. Subsequently, animals were inoculated with filtrates of cultures of these bacteria and a comparison of the pathologic changes produced by the inoculation of the bacteria themselves and of their toxins was made.

They state that Cornil and Babes had called attention to the favorable arrangement of the vessels in the glomeruli for the retention of microorganisms. The fact is also emphasized that after bacteria can no longer be discovered in the kidneys, the changes provoked by them may continue to progress.

Their final conclusions are: First, That in cases of general infection, the passage of bacteria through the kidneys produces

various anatomic and pathologic changes in the kidney structure.

Second, The totality of the changes produced by the anthrax bacillus, the bacillus pyocyaneus and the staphylococcus pyogenes aureus furnish a conclusive and positive experimental proof of the production by these bacteria of a glomerulonephritis.

Third, This form of nephritis attacks particularly the cortical structure and only to a limited extent the medullary.

Fourth, The pathologic process begins as an endarteritis with disturbances of circulation inducing hæmorrhages and then causes alterations in the Malpighian glomeruli, Bowman's capsules and the epithelium of the convoluted and straight uriniferous tubules.

Fifth, With alteration of the epithelium occurs exfoliation and occlusion of the tubules, agglutination of the walls resembling hyperplasia of the intertubular connective tissue. In the event of a cure there is a reconstruction of the tubules and a regeneration of tissue.

Sixth, In the pathogenesis of this form of nephritis the bacteria which produce the general infection are the most important factors, but as excitants of the process the toxins of these bacteria play an important role; and in the event of their virulence or great abundance these toxins are alone capable of exciting the diseased process even to a severe degree, provided they enter the blood and reach the kidneys.

It appears then, that in nature's effort to throw off the existing infection, the kidneys which are called upon in part to excrete the same, become a receptacle of bacteria and their toxins, which having been conveyed through the arterial blood to the glomeruli in the renal cortex, are transuded into the surrounding capsule of Bowman and thence into the uriniferous tubules. For this reason this form of nephritis particularly affects the cortex, and only to a limited extent the medullary structure of the kidneys.

Dr. Geo. Sittman⁴ at a later period, and he says without knowledge of the work of Pernice and Scagliosi, carried on

pathologic studies of a similar nature directed particularly to the excretion of staphylococci by the kidneys. He gives in detail his method of injection of the germs into the circulation and states that he established the identity of those obtained in the kidneys and urine by cultures on gelatine and agar as well in bouillon. He determined furthermore their pyogenic character by the inoculation of the anterior chamber of the eyes of rabbits. He reviews the work of other investigators and shows that, while in the course of an infectious disease nature attempts to rid herself of the infection through the skin and various secretions as the milk and bile, it is the kidneys which must particularly assume the burden of carrying off the infection. He contends that he has demonstrated by a number of experiments that pathologic staphylococci can appear in the urine when the lesion is not only slight, but where apparently no damage at all has been done to the kidneys. His experiments were largely upon rabbits. Careful examination of the urine was made to determine whether the microorganisms were present in the urine or only in the blood which had been excreted with the urine. Based upon fifteen experiments the conclusions drawn are that staphylococci circulating in the blood are excreted by the kidneys; that the extent of the appearance of these microorganisms in the urine depends upon the virulence of the infection; that while in milder infections their secretion may cease at the end of fourteen hours, in the severe ones they continue at least forty-six hours and in extreme cases until the death of the animal; that both microorganisms and the toxins are thus eliminated.

In the same volume appears an article by Engel on "*Experimentelle Untersuchungen ueber Bacteriurie bei Nephritiden.*" This article contains a summary of the labors of a good many different investigators to which only reference need be made. It also includes the work of the author based upon the study of thirty-one cases of nephritis occurring in both sexes.

A specific coccus is described to which is attributed the occurrence of a primary form of bacterial nephritis. This was

found seventeen times. A similar claim for the existence of a particular bacillus capable of provoking a definite form of primary bacillary nephritis was made by Letzerich ⁶ as long ago as 1887.

Engel also discovered the staphylococcus pyogenes albus and aureus sixteen times, a streptococcus which rendered bouillon turbid six times, one which rendered it clear twice, the tubercle bacillus four times, the typhoid bacillus once, the bacillus coli communis five times, while bacteria were absent but twice. In his conclusions he quotes Neuman ⁸ and endorses his statement that "despite the presence of bacilli in the kidneys these cases are not of bacterial, but of toxic origin."

An interesting summary of the effect of the injection of the filtered cultures of staphylococci upon the kidneys can be found in the work of Kolle and Wasserman, Bd. III. The changes described are attributed to a coagulation necrosis dependent upon the production of an infarct and the destruction of the leukocytes due to the production of leukocidin. The kidneys were alike affected whether the toxins were introduced into the pleural or peritoneal cavity or into the veins. Minute abscesses ranging from the size of a pinhead to that of a pea were found in the kidneys, particularly in the cortex. Leukocidin could only be produced when hemolysin was present, yet it seems to be proven that they are two entirely distinct poisons.

The investigations along this line have not been very numerous in this country. In 1897 Councilman ⁷ published an anatomical and bacteriological study of forty-nine cases of acute and sub-acute nephritis with special reference to the glomerular lesions. He argues that the most scientific classification of kidney diseases is one based on the etiology, but states that the time is not ripe for the adoption of such a classification. While in general septicaemia, bacteria have been discovered in the kidneys, he states that various microorganisms have produced apparently the same pathologic changes in these organs and the same organisms seem to be associated often with widely different anatomic lesions. He believes that all lesions positively

dependent upon bacteria are focal; the changes they produce in the kidney being in the immediate sphere of the bacteria. The diffuseness of a kidney lesion he argues indicates its dependence upon substances in solution in the blood, namely, the chemical products of bacteria. Moreover, he calls attention to the toxins which are produced in the gastro-intestinal tract, stating, "that chemical substances may be produced in the alimentary canal or by the imperfect action of some organ in the body which may exert a deleterious action on the kidneys."

A very interesting and thoroughly scientific discussion of nephritis was held by the Chicago Academy of Medicine, February 10, 1899.⁸ The papers of Drs. Preble, Walls, Turk and Wesemer are worthy of our careful study. The biochemistry of the various toxic products and their effect upon the kidneys was considered. The effect upon the kidneys of those toxic substances produced in the digestive tract was discussed. It was asserted that atony or arrested function of the gastro-intestinal tract invariably results in the retention of materials which undergo decomposition and then affect the kidneys because of their toxic character.

That cases of bacterial or toxic nephritis present rather a favorable prognosis if the primary disturbance can be relieved appears in a paper by Mannaberg.⁹ In eleven cases which he believed to be of streptococcic origin the germs were found present in the urine in eight. Of the eleven cases seven recovered, one improved and three died. His paper also contains a statement of his experimental work.

As bearing upon this question I report three cases. The first one presumably of staphylococcic infection, in which the patient suffered from septic endocarditis as well as nephritis; the second a case of intestinal obstruction without septic disturbance of any kind and in which in consequence of the complete arrest of intestinal function a very serious and all but fatal form of nephritis was awakened; the third in which there was, complicating gall-stone disease, a sub-acute pancreatitis, and in consequence of the disturbance of the secretory function of this gland a toxic condition was aroused, causing not only nephritis

but also glycosuria. In each of the three cases after removal of the causal condition all evidence of renal disease disappeared.

CASE I.—*Sloughing submucous fibroids; septicæmia; endocarditis; nephritis; expulsion of fibroids; subsidence of septic manifestations; recovery.*

Miss L.; aged forty; school teacher; unmarried; consulted me March 1, 1896. There was a negative family and personal history. Since December, 1896, she had suffered from profuse menstruation unattended by pain. The flow continued usually for ten days. An examination made by Dr. Juliet E. Hanchett showed that she was suffering from fibroid tumors of the uterus. Radical operation was refused and expectant treatment with medication and electricity was instituted.

I saw her again fourteen months later, namely, in May, 1899, when she reported a very marked improvement as to the hæmorrhage. The uterus had, however, increased in size and reached nearly to the umbilicus. I did not see her again until September 6, 1901, at which time the uterus reached fully as high as the umbilicus; was a hard, irregular mass; but freely movable.

When I was next called to see her, September 8, 1905, she was at the Syracuse Hospital for Women and Children, suffering from profound sepsis. She had been spending her vacation on Oneida Lake and had returned home three weeks before feeling exhausted and suffering from fever and diarrhœal movements.

When Dr. Charles F. Wiley was called he found her menstruating. The flow was very profuse; it was of dark color and had an offensive odor. In the discharge there were small pieces of pale tissue. The spleen was slightly enlarged; the skin was jaundiced, as were also the conjunctivæ. There were systolic murmurs to be heard over the entire præcordial area. The diarrhœa continued about ten days. The blood was examined on August 24. The Widal reaction was negative. At this time each cubic millimeter contained 4,200,000 red and 20,000 white cells, while the hæmoglobin percentage was 47.

During this period there were sharp remissions of temperature. The morning recession would be about to normal, the evening rise from 103.2 to 105.4 degrees F. The pulse rate during this period was from 90 to 100. At this time the urine was repeatedly examined and found to be amber, cloudy, acid, had a

specific gravity usually of 1028, contained no sugar but had a large percentage of albumin and microscopically hyaline and granular casts, epithelial cells, red blood and pus cells were found. For the purpose of examination the urine was drawn by catheter. The vaginal discharge was profuse, and repeated examinations bacteriologically discovered each time the staphylococcus pyogenes aureus.

On September 7 the patient expelled from the uterus with severe pain a mass which was sent to the pathologist, Dr. Steensland for examination. His report was as follows:

"The specimen has two flattened surfaces; is nearly circular. Its surface is very irregular, presenting depressions and elevations. It measures 6.3 by 5 by 3 cm. and weighs 43 grammes. It is elastic to the touch, but in some parts more firm. Its general color is white with yellowish semi-plastic material on the surface in some places. On section the cut surface shows numerous blood vessels and bands of dense fibrous tissue separating the irregular areas of reddish softer tissue. The parts firm to the touch, as mentioned above, contain relatively more fibrous tissue than the elastic parts. Diagnosis, necrotic leiomyoma."

With the expulsion of the growth, the temperature fell so that for two days it did not go above 102.6. Pus was discharged more profusely.

This was the condition when I saw her on September 8, 1905. The anæmia was very striking. There was extreme pallor of the mucous membrane, while the complexion was very sallow. Examination of the surface of the body did not show any petechiæ. There had been no hæmorrhage from any organ. Over the entire præcordial area loud blowing murmurs could be heard. The uterus reached above the level of the umbilicus. The uterine cervical canal was sufficiently patent to receive my index finger and the presence of a soft mass occupying the cavity of the uterus could be readily made out. Blood examination showed a leukocytosis of between 22,000 and 23,000 and the hæmoglobin had fallen to 40 per cent. The urine was loaded with albumin and casts. The pulse ranged from 90 to 100. During the next few days the temperature each afternoon was between 103 and 104, while that of the morning was normal. She suffered daily from recurring chills and profuse sweats.

On the thirteenth her condition not improving I placed her

upon the operating table and found an enormous mass trying to deliver itself from the uterine cavity. I attempted to stretch the already dilated cervix sufficiently to permit it to expel the tumor but my efforts were ineffectual. Because of the septic condition I did not deem it wise to make a section of the cervix. I introduced a flushing curette for the purpose of washing out the uterus. Immediately upon its introduction there was a discharge of at least a pint, if not a quart of stinking pus. The uterus was then washed out. A heavy rubber drainage tube was introduced for the double purpose of permitting drainage and stimulating the uterus to contraction. In consequence, not only was the uterus drained of pus but three days later the patient expelled another tumor more than twice the size of the former one and of the same character. The temperature fell at once to normal and there was no further recurrence of fever. Immediately improvement in her general condition became apparent. She was able to take food. The blood improved in character so that three and one-half weeks later when she was dismissed from the hospital a blood examination showed 4,968,000 red and 12,000 white cells to be present and the hæmoglobin to have come up to 75 per cent.

On September 22, the urine still contained a trace of albumin, but no casts. On October 21, 1905, the urine was straw colored, clear, acid, 1020, contained no albumin nor sugar, earthy phosphates were normal, total 8 per cent.; microscopically there were a few squamous epithelia and amorphous urates. At that time I found the heart sounds normal. Bi-manual examination of the uterus showed it to be slightly enlarged reaching just above the pubis and the fundus soft. There was a small fibroid, at the junction of the cervix with the fundus on the anterior wall. The tubes were normal. Since then she has continued to remain in perfect health. The urine has been repeatedly examined and every time found to be normal.

CASE II.—*Intestinal obstruction due to adhesions and bands; pronounced nephritis; uræmic convulsions; recovery.*

Mrs. W., a resident of Johnson City, Tennessee, was called to her mother's home in Cazenovia, N. Y., on January 9, 1906. She was forty-five years of age, the mother of three children, the oldest 23 and the youngest 10. There was a negative family history.

For more than 25 years she had been having recurring attacks of severe constipation amounting almost to complete obstruction, but each time was relieved by cathartics and enemata.

On her way north she was seized with severe abdominal pain and distress. Upon her arrival in Cazenovia on the evening of January 5, Dr. Walsh of that village was called to see her. He gave her a hypodermic injection of morphine to relieve her pain. On the following day, January 6, she vomited continuously, the vomited material, however, being of bilious character. No movement of the bowels could be obtained. On January 7, the vomiting still persisted. During the morning it was greenish in color but in the afternoon it became stercoraceous. Saline and other cathartics as well as enemata had been given her without avail. Her condition grew steadily worse until I saw her on the morning of January 9, 1906. At that time I found the pulse 120 and very feeble, no fever, marked distention of the abdomen, some sensitiveness over the right side but no rigidity. The facilities for operation there were poor, and so she was placed upon a cot-bed and brought by train a distance of more than twenty miles to St. Joseph's Hospital, Syracuse. This was at mid-day. A specimen of urine obtained by catheterization upon her arrival at the hospital was found to be amber, acid, sp. gr. 1022, contained no sugar, 5 per cent. of albumin by the ferrocyanide test, hyaline and granular casts, squamous epithelium as well as round and spindle cells and granular debris. A tube was introduced into the stomach, and about a pint of thin faecal matter was withdrawn. The pulse in the meantime had become so feeble and the respirations so shallow that it was impossible to give the patient a general anæsthetic. An intravenous injection of the normal salt solution was therefore administered. This improved the condition at once, so that I could operate, being assisted by Dr. Flaherty.

On opening the abdomen the presenting intestines were found to be darkly congested. There was some bloody serum in the abdominal cavity. The obstruction was found to be in the right iliac fossa, where a broad band connected with a very large ovarian mass was found under which a loop of gut had become twisted in the shape of a figure eight. The band was cut and the ovarian tumor removed. Various other bands of adhesion not directly concerned in the obstruction were severed. The abdomen was closed without drainage. Six ounces of deci-

normal salt solution, with two of whiskey were given per rectum as well as caffeine, spartein and digitalis hypodermically. She continued to vomit frequently until three o'clock on the following day. The vomited material was of fecal character during the night, but in the morning became bilious. The bowels moved voluntarily twice on the day after the operation. The urine was of sufficient quantity during the first twenty-four hours but was highly albuminous and contained hyaline and granular casts. The only serious symptoms the patient experienced after operation were due to the renal condition.

On January 12 the urine became much less abundant and still contained six per cent. of albumin, had a sp. gr. of 1030, and casts were very numerous. During the night between the twelfth and the thirteenth the urine became practically suppressed, and on the following morning we were confronted with a condition of anuria associated with evidences of uræmic toxæmia. At my request the house surgeon gave the patient another intravenous injection of normal salt solution and an hour later the pulse improved and the urine was again excreted, although the patient had a general convulsion of uræmic character in the meantime. Dr. Elsner, who saw her in consultation with me, suggested the use of digalen. Large quantities of the decinormal salt solution were also given per rectum with the cistern placed just above the level of the bed. A satisfactory discharge of urine resulted, but the percentage of albumin did not vary much from $4\frac{1}{2}$ to 6 per cent. The sp. gr., however, became somewhat lower, ranging from 1018 to 1020. There was always a large number of casts and usually leukocytes and red blood cells present.

On the thirteenth, 7 per cent. of albumin was recorded with a sp. gr. of 1010. On the following day it was but 3 per cent. and after that the sp. gr. ranged only from 1006 to 1010. The percentage of albumin was not, however, materially reduced nor were the casts less evident until January 25, namely, sixteen days after operation. There followed a very rapid change, and four days later the albumin had entirely disappeared as had also the casts. The sp. gr. continued very low, rarely exceeding 1010 for the next two weeks, but after this date it, as well as the other features of the urine, became normal and continued so. The patient returned to her home in Tennessee, and as far as I have been informed has remained perfectly well.

CASE III.—*Cholecystitis with gall-stones; sub-acute pancreatitis associated with nephritis and glycosuria; operation; recovery.*

Mrs. B., aged thirty; seen in consultation with Dr. Levy, November 21, 1906. She had a history of gall-stone disease covering a period of six years. Her present attack was of five weeks duration. During this time she had been quite prostrated, suffering continuously, and required the frequent administration of morphine hypodermically. There was no fever; jaundice was marked; tenderness over the gall-bladder was considerable. A specimen of urine drawn by catheter was found to be of dark amber color, clear, sharply acid, 1032, contained two per cent. of albumin and two and one-half per cent. of sugar, some bile, total phosphates eight per cent., earthy phosphates normal; microscopically a great abundance of squamous epithelia, a large number of both hyaline and granular casts, some pus cells and uric acid. She was admitted into St. Joseph's Hospital and observed for a few days, but her condition did not improve. The urine on repeated examination was found to present the same characteristics.

On November 25, assisted by Dr. Flaherty, I operated upon the patient. The gall-bladder was found to be somewhat distended with bile, which on subsequent bacteriologic examination was found to contain the bacillus coli communis. A single gall-stone was present. It was removed. The gall-bladder was implicated in a hard infiltrating mass which included the common duct and the pancreas. The latter gland was quite hard and firmly adherent to the surrounding structures. A drainage tube was introduced into the gall-bladder and the wound closed. Gauze tapes were packed around the gall-bladder at points where the tissue had been torn by manipulation. While the gauze tapes remained the patient had an irritable stomach and vomited considerably, but upon their withdrawal the vomiting ceased. For the next twenty-four hours the urinary excretion amounted to 24 ounces; during the second to 20 ounces. Digalen, citrate of potassium and saline cathartics were prescribed and fluids both by mouth and rectum freely administered; for the latter purpose the decinormal salt solution being used. The urine on November 30 was found to be dark amber, clear, acid, had a sp. gr. of 1030, still contained bile, total phosphates were 12

per cent., earthy phosphates normal and both sugar and albumin had disappeared; there were a few crystals of uric acid and an occasional hyaline cast. On December 3 the urine was entirely normal. From this time on the patient continued to steadily improve. Drainage of the gall-bladder was kept up for five weeks, at the end of which time the wound was ready to close, and did promptly. The urine continues normal and there is no evidence of any renal disturbance.

The subject of nephritis, dependent upon truly surgical conditions located quite remotely from the kidneys, is one to which not sufficient attention has been given by the profession, at least in this country.

In our first case we had a bacterial or toxic nephritis dependent upon a septic condition and associated with other evidences of profound sepsis, especially the changes in the heart. The patient's condition was exceedingly precarious, and yet after the expulsion of the fibroids and the subsidence of the sepsis of the uterus, there was at once a prompt recovery from the secondary disturbance both in the heart and kidneys.

In our second case, evidently the result of interruption of intestinal function, a toxic condition was created within the intestinal tract and, as a result of this toxæmia, we had a pure toxic nephritis. This was so extreme that we were confronted by a graver danger after having relieved the acute intestinal obstruction. The patient's life was almost extinguished in consequence of the nephritis. Here also the nephritis was cleared up by the relief of the surgical condition.

Our third case presents still another phase, namely, one in which a large secretory gland, because of its inflamed condition due to gall-stone disease, created a toxic condition which awakened not only toxic nephritis but glycosuria as well. In this case the subsidence of the nephritis disturbance was even more prompt than in the other two cases.

It is generally held that the presence of nephritis is to be regarded as a possible and oftentimes a serious contraindication to surgical operation. It seems to me that in the class of cases presented for your consideration in this paper the bacterial or

toxic nephritis becomes rather a most positive indication for operation, as by such a course only can it be relieved.

REFERENCES.

- ¹ Vulpian. Leçons sur la bile.
- ² Gouget. Nov. 30, 1895, Du rôle de l'auto-intoxication dans la pathogénie des néphrites.
- ³ Pernice and Scagliosi. Virchow's Archiv, 1894, Bd. cxxxviii, S. 521
- ⁴ G. Sittman. Arbeiten aus dem Medizinisch Klinischen Institute der K. Ludwig-Maximilian's Universität zu München; Ziemmsen u. Bauer, Bd. iv, S. 51, 1899.
- ⁵ Letzerich. Zeitschr. für klin. Medicin, Bd. xiii, S. 33.
- ⁶ Neuman. Berliner klin. Wochenschr., 1890, No. vi.
- ⁷ Medical and Surgical Reports of the Boston City Hospital, 1897.
- ⁸ Journal of the American Med. Association, March 11, 18, and 25, 1899.
- ⁹ Mannaberg. Zeitschrift für klin. Medicin, Bd. xviii, S. 223, 1890.